Ondansetron Prescription Is Associated With Reduced Return Visits to the Pediatric Emergency Department for Children With Gastroenteritis

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Study objective: We determine whether an ondansetron prescription for pediatric patients with vomiting or gastroenteritis is associated with decreased return visits to the emergency department (ED), and whether alternate diagnoses are more frequent on return visits in patients prescribed ondansetron.

Methods: This is a retrospective cohort study of patients 6 months to 18 years of age, presenting to a pediatric ED or its affiliated urgent care centers between 2012 and 2017 with an *International Classification of Diseases, Ninth Revision* or *International Statistical Classification of Diseases and Related Health Problems, 10th Revision* diagnosis of gastroenteritis, gastritis, vomiting, or vomiting with diarrhea. Multivariate logistic regression analysis was used to measure the association between an ondansetron prescription and the odds of 72-hour return visits. Rates of alternate diagnoses on return visits (appendicitis, intussusception, intracranial mass, meningitis, and diabetic ketoacidosis) were compared between patients who were prescribed ondansetron for home use and those who were not.

Results: A total of 82,139 patients were studied, with a median age of 4 years. An ondansetron prescription was given to 13.4% of patients on discharge. The 72-hour return visit rate was 4.7%. Patients receiving an ondansetron prescription had decreased odds of 72-hour return visits (adjusted odds ratio 0.84; 95% confidence interval 0.75 to 0.93). The subgroup of patients specifically receiving a diagnosis of gastroenteritis had decreased odds of 72-hour return visits (adjusted odds ratio 0.82; 95% confidence interval 0.72 to 0.95). There was no significant difference between groups in the diagnosis of appendicitis on return visit (odds ratio 0.97; 95% confidence interval 0.37 to 2.18).

Conclusion: An ondansetron prescription is associated with reduced 72-hour ED return visit rates for children with vomiting or acute gastroenteritis and is not associated with masking alternate diagnoses. [Ann Emerg Med. 2020;■:1-10.]

Please see page XX for the Editor's Capsule Summary of this article.

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INTRODUCTION

Background

Acute gastroenteritis is one of the most common reasons for emergency department (ED) visits in the United States.[1] It accounts for approximately 1.5 million pediatric outpatient visits and 200,000 admissions every year.[2] The mainstay of care for gastroenteritis is supportive treatment, relying on rehydration therapies and antiemetic use, of which the most studied is ondansetron.[3] It has been shown to reduce vomiting in pediatric patients with gastroenteritis, facilitate oral rehydration in the ED, and decrease hospitalization rates.[4-6] Because of its effectiveness in controlling vomiting, ondansetron use has significantly increased during the past decade and in 2017 was the most commonly used drug in US emergency departments.[7] Despite its current routine use in managing acute vomiting during ED visits, there are limited studies assessing the potential effect of an ondansetron prescription after discharge.[8,9]

There are significant variations in practice among physicians as it relates to prescribing ondansetron for patients to use at home after discharge from the ED. Many physicians cite fear of masking symptoms of an alternate diagnosis such as appendicitis as their reason for not prescribing ondansetron for home use. We have unpublished data from our institution that show a marked variation in the rates of ondansetron prescriptions among individual physicians. Of the 28 pediatric emergency medicine physicians working in the ED, prescription rates ranged between 5.1% and 54.6%, and of the 58 pediatricians working in the urgent care centers, rates were also variable, ranging between 0% and 86%.

Editor's Capsule Summary

What is already known on this topic

Ondansetron decreases hospital admission and intravenous fluid use for children visiting the emergency department (ED) for gastroenteritis or vomiting.

What question this study addressed

Does an outpatient prescription for ondansetron affect rates of return visits for children discharged from the ED for vomiting or gastroenteritis?

What this study adds to our knowledge

This historical cohort study reported that children prescribed ondansetron had a lower probability of returning to the same ED in the following 72 hours (adjusted odds ratio 0.84; 95% confidence interval 0.75 to 0.93; number needed to treat to benefit=138).

How this is relevant to clinical practice

Outpatient ondansetron may be a reasonable choice for children discharged from the ED for gastroenteritis. A randomized trial is needed.

Importance

Variations in practice may lead to differences in return visit rates, which may have implications for patients and families, as well as for the health care system.[10] Return visit rate is currently considered a quality-of-care metric and represents 2.7% to 8.1% of total visits to the pediatric ED,[11] with one of the most common reasons being persistence of symptoms.[12] Vomiting accounts for a large proportion of pediatric ED visits nationally; thus, the associated number of revisits related to this complaint is significant.[7] This may add to the increasing problem of ED crowding, which can lead to medical errors, increase in length of stay, and decrease in patient satisfaction.[13]

Goals of This Investigation

The primary objective of our study was to evaluate whether a prescription for ondansetron on discharge from the pediatric ED or urgent care center in patients with vomiting or gastroenteritis was associated with a difference in return rates within 72 hours. We had 2 secondary objectives. The first was to evaluate the association between an ondansetron prescription and return rates in patients specifically receiving a diagnosis of gastroenteritis. The second was to assess whether there is an association between an ondansetron prescription and alternate diagnoses on return visits.

MATERIALS AND METHODS

Study Design and Setting

We conducted a retrospective cohort study of pediatric patients who presented to a large, urban, tertiary care, pediatric ED and its 11 affiliated urgent care centers during a 5-year period between April 2012 and December 2017, with a diagnosis of vomiting or gastroenteritis, according to *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9)* or *ICD-10* billing codes. The combined sites treat greater than 210,000 patients per year and are part of the largest pediatric health care system in the county. This study was approved by the hospital's institutional review board as an exempt protocol.

Selection of Participants

Patients were eligible for inclusion if they were between 6 months and 18 years of age, had an index visit to the ED or urgent care center, and were discharged home with one or more of the following diagnoses: gastroenteritis (K52.9, A08.4, A09, 558.9, 009.0, 009.1, and 008.8), vomiting and diarrhea (R11.10, R11.2, R19.7, and 787.91), vomiting alone (R11.1, 787.01, 787.02, 787.03, 536.2, and 078.82), or gastritis (K29.70, 535.00, 535.40, and 535.50) according to *ICD-9* or *-10* (2012 to 2015 and 2015 to 2017, respectively) billing codes. Additionally, we included patients with dehydration (E86.0, R63.8, and 276.51) only if there was an associated diagnosis of vomiting, with or without diarrhea. We did not, however, include patients with a diagnosis of diarrhea without vomiting. See Appendix E1 (available online at http://www.annemergmed.com) for the list of diagnoses and their associated billing codes, as well as details of how the groups were defined. An index visit was defined as one for which there was no other ED or urgent care center visit in the preceding 30 days. Patients admitted to the hospital or with missing disposition during their index visit were not eligible for inclusion, and neither were those with what the authors considered a priori to be relevant preexisting medical conditions (see Appendix E2 [available online at http://www.annemergmed.com] for the list of preexisting medical conditions). We did not include patients younger than 6 months because ondansetron is not typically used for this age group at the study institution.

Methods of Measurement

We used the health system's electronic data warehouse to collect clinical and demographic information on all

patients with the *ICD* codes of interest. Demographic data comprised age; sex; race; ethnicity; primary language; date, time, and location of visit (ED versus urgent care center); and type of health insurance. Clinical data included Emergency Severity Index (ESI) level; preexisting medical conditions; length of stay; radiologic studies obtained, including type of study; medications received during visit, including route of delivery; intravenous fluid bolus administration; home prescription for ondansetron; other home prescriptions electronically ordered; and 72-hour and 1-week return visits, with their associated diagnoses. After data collection, a chart review was performed by the primary author (D.B.) on 100 randomly selected patient charts to ensure accuracy and consistency of the data, and patients' charts perfectly matched the results obtained from the electronic data warehouse. We then removed from the data set patients who did not meet age criteria, those who were admitted to the hospital during their visit, and those who had the predetermined medical conditions. We subcategorized patients with a specific diagnosis of gastroenteritis (*ICD* code of either gastroenteritis or a combination of *ICD* codes for vomiting and diarrhea) for separate analysis (detailed later). We then deidentified our data set before statistical analysis.

The following 15 variables, as recorded during the index visit, were considered a priori to be potential confounders for the association between the exposure and the outcomes of the study: age, sex, race, ethnicity, type of health insurance, site of the visit (ED versus urgent care center), treating physician (pediatric emergency physician versus pediatrician), Emergency Severity Index level (categories 1 to 5), length of stay, and any of the following ordered or given during the visit: intravenous access (yes/no), intravenous fluid bolus (yes/no), medications (yes/no), ondansetron (yes/no), diagnostic imaging orders (yes/no), and home prescriptions (yes/no). Of these variables, 7 were considered a priori to be proxies of severity of illness during the index visit; they included Emergency Severity Index level, length of stay, intravenous access, intravenous fluid bolus, diagnostic imaging, and medications given during the visit, including ondansetron.

Outcome Measures

The primary outcome was the rate of return visits to the ED or urgent care center within 72 hours for patients with vomiting or gastroenteritis. We did not make a distinction between scheduled and unscheduled return visits because there is no institutional protocol to have scheduled return visits to the ED for these conditions. Outcomes for the secondary objectives were the rate of return visits to the ED or urgent care center within 72 hours in the subgroup of patients with gastroenteritis, and the rates of select alternate diagnoses (appendicitis, intussusception, intracranial mass, meningitis, and diabetic ketoacidosis) on return visits within 7 days. We chose these 5 alternate diagnoses in accordance with the potential of their mimicking vomiting caused by gastroenteritis or other viral illness early in the disease process, and extended the return visit to 7 days to be able to capture alternate diagnoses that might present within this period.

Primary Data Analysis

The distributions of the population baseline characteristics were compared according to the exposure of interest, which was receiving a prescription for ondansetron at discharge from the index visit. A bivariate analysis was conducted to assess the association between receiving a prescription for ondansetron and the 72-hour return visit rate, according to baseline characteristics. The association between normally distributed continuous variables and the primary outcome was assessed to obtain the difference between means, along with 95% confidence interval (CI). Differences between proportions and odds ratios (ORs) with 95% CI were used for categoric variables.

Multivariate logistic regression analysis was used to measure the association between receiving a prescription for ondansetron and the frequency of 72-hour return visits to the ED or urgent care center while adjusting for covariates and potential confounders. Predictors that showed no statistically significant association with the exposure or with the outcome in the bivariate analysis or that had a strong and significant correlation with other predictors (correlation coefficient >0.25 or <-0.25) were considered candidates to be omitted from further analysis (Appendix E3, available online at http://www.annemergmed.com). Ultimately, in addition to the exposure of interest (ondansetron prescription given on discharge), 8 of the 15 covariates were retained for entry into the multivariate analysis: age, race, intravenous fluid bolus, ondansetron given during visit, radiologic study, insurance type, location of visit (ED versus urgent care center), and treating physician (pediatric emergency medicine physician versus pediatrician). The other 6 covariates were omitted because they were not associated with the exposure or the outcome, or because of collinearity with variables already included in the model. Specifically, Emergency Severity Index level was omitted because it was not associated with the outcome in the unadjusted analysis. Only one covariate (radiologic study) that did not show significant association with the exposure in the bivariate analysis was retained, given

that it was considered a proxy for severity of illness at baseline. The goodness of fit of the model was assessed with the Hosmer-Lemeshow test.

We performed similar analysis on the subgroup of patients specifically receiving a diagnosis of gastroenteritis. Finally, we explored whether receiving a prescription for ondansetron was associated with an increased risk of diagnosing appendicitis, intussusception, intracranial mass, meningitis, or diabetic ketoacidosis during the return visit compared with not receiving one. All analyses were conducted with SPSS (version 20.0; IBM Corp, Armonk, NY).

RESULTS

Characteristics of Study Subjects

During the study period, 109,222 patients met the search criteria by *ICD-9* and *-10* diagnoses. Of these patients, 24.4% were not eligible for inclusion in the study (3.7% were <6 months or >18 years, 9.5% were admitted to the hospital during the index visit, and 11.2% were identified as having relevant preexisting medical problems) (Figure). There were 82,575 eligible patients who entered the study. After exclusion of 436 patients with a missing disposition, the final study sample was 82,139. Additionally, 5,445 eligible patients (6.6%) had to be excluded from the multivariate analysis because of missing data on at least one of the covariates included in the model. Given the relatively small fraction of patients excluded for this reason, no imputation techniques were used.

Approximately half of the patients were male. Most patients (86.3%) were white, 7.7% were black, and 6% were of other or unknown race. Patients of Hispanic ethnicity accounted for 84.9% of the sample. The majority of patients (69.7%) had Medicaid as their primary insurance. Most of the index visits (58.9%) were to the ED and 22.3% of patients were treated by a pediatric emergency medicine–trained physician. An intravenous fluid bolus was given to 7.9% of patients, ondansetron was administered during the visit to 55.1% of them, and a radiologic study was ordered for 13.5% of them.

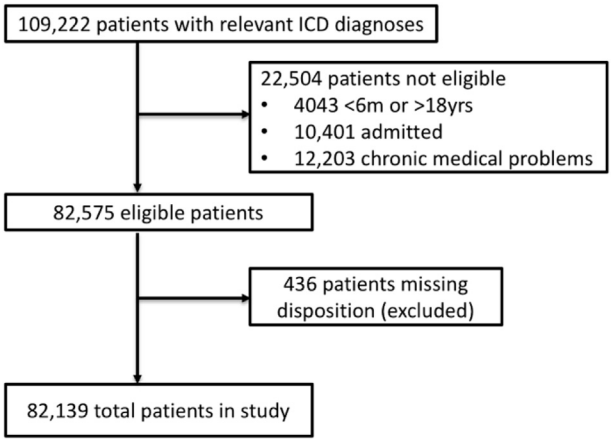

Figure. Flow diagram with the patients included or excluded from the study.

An ondansetron prescription at discharge was given to 11,004 patients (13.4%). Table 1 compares the baseline characteristics between patients receiving a prescription for ondansetron and those who did not. Significant differences were found for almost all baseline characteristics; however, several of these statistical differences could be attributed to the large sample size and may be clinically unimportant, given the small absolute differences. Patients who received an ondansetron prescription were older than those who did not. Medicaid insured, black, and non-Hispanic patients were less likely to receive an ondansetron prescription.

Main Results

Three thousand eight hundred fifty-one patients (4.7%) had a return visit within 72 hours. Receiving a prescription for ondansetron was associated with reduced odds of 72-hour return visits (unadjusted OR 0.84; 95% CI 0.76 to 0.92) (Table 2). Patients who were treated by a pediatric emergency medicine–trained physician (versus pediatrician) also had a decreased risk of return within 72 hours, as well as patients who were black (versus white patients). On the other hand, there was an increased risk of return in Hispanic patients versus non-Hispanic ones, those receiving an intravenous fluid bolus, those who had a radiologic study performed, those who had ondansetron given during visit, and those who were treated in the ED (versus urgent care center).

After adjustment for the covariates and potential confounders, receiving an ondansetron prescription remained significantly associated with the outcome, with a reduction in the odds of 72-hour return visits (adjusted OR 0.84; 95% CI 0.75 to 0.93) (Table 3). Other covariates that remained statistically associated with 72-hour return visits after adjustment were younger age, black race, receiving an intravenous fluid bolus, being treated by a pediatric emergency medicine–trained physician, ondansetron given during index visit, a radiologic study obtained during visit, and being treated in the ED (Table 3). Table E1 (available online at http://www.annemergmed.com) shows the details (variables and values) of the logistic regression equation, as well as the goodness of fit of the model.

Table 1. Comparison of baseline characteristics between patients who received an ondansetron prescription at discharge and those who did not.

Characteristic	Ondansetron Prescription, N = 11,004	No Ondansetron Prescription, N = 71,135	Difference (95% CI)
Age, y			
Median (IQR)	5.0 (3 to 9)	4.0 (2 to 7)	NA
Mean (SD)	6.4 (4.5)	5.1 (4.3)	1.3 (1.2 to 1.4)
LOS, mean (SD), min	176.0 (95.2)	157.9 (114.6)	18.1 (15.8 to 20.4)
Female sex	5,543 (50.4)	34,890 (49.0)	1.4 (0.3 to 2.3)
Hispanic ethnicity	8,864 (83.4)	58,647 (85.2)	−1.8 (−2.6 to −1.0)
Race			
White	9,314 (88.4)	58,759 (84.7)	3.7 (3.0 to 4.4)
Black	569 (5.4)	5,477 (7.7)	−2.5 (−3.0 to −2.1)
Other/unknown	648 (6.2)	4,113 (6.0)	0.2 (−0.3 to 0.7)
IV access obtained during visit	1,504 (13.7)	6,279 (8.8)	4.8 (4.2 to 5.5)
IV fluid bolus given during visit	1,334 (12.1)	5,149 (7.2)	4.9 (4.2 to 5.5)
Any medications given during visit	7,695 (69.9)	40,534 (57.0)	13.0 (12.0 to 13.9)
Ondansetron given during visit	8,234 (74.8)	36,996 (52.0)	22.8 (21.9 to 23.7)
Any prescription at discharge	11,004 (100.0)	24,090 (33.9)	66.1 (65.8 to 66.5)
Radiologic study during visit	1,437 (13.1)	9,667 (13.6)	−0.5 (−1.2 to 0.1)
ESI level			
1	0	1	NA
2	66 (0.7)	413 (0.8)	−0.07 (−0.26 to 0.1)
3	2,792 (30.7)	11,956 (23.2)	7.6 (6.6 to 8.6)
4	6,199 (68.2)	39,108 (75.7)	−7.5 (−8.6 to −6.5)
5	2	8	0.007 (-0.03 to 0.04)
Missing	27 (0.3)	148 (0.3)	0.01 (-0.1 to 0.1)
Insurance			
Medicaid	6,919 (65.2)	48,710 (70.4)	−5.3 (−6.2 to −4.3)
Commercial	3,163 (29.8)	17,480 (25.3)	4.5 (3.6 to 5.4)
State	249 (2.3)	1,168 (1.7)	0.7 (0.4 to 1.0)
Self-pay	289 (2.7)	1,822 (2.6)	0.09 (−0.2 to 0.4)
Treated in the ED (vs UCC)	8,066 (73.3)	40,436 (56.7)	16.5 (15.6 to 17.4)
Treated by a pediatric **emergency** medicine physician (vs pediatrician)	3,203 (29.1)	15,104 (21.2)	7.9 (7.0 to 8.8)
Year of visit			
2012	777 (7.1)	8,468 (11.6)	−4.8 (−5.4 to −4.3)
2013	1,449 (13.2)	11,490 (16.2)	−3.0 (−3.7 to −2.3)
2014	2,193 (19.9)	12,654 (17.8)	2.1 (1.3 to 2.9)
2015	2,410 (21.9)	13,331 (18.7)	3.2 (2.3 to 4.0)
2016	2,332 (21.2)	12,981 (18.2)	2.9 (2.1 to 3.8)
2017	1,843 (16.7)	12,211 (17.2)	−0.4 (−1.2 to 0.3)

IQR, Interquartile range; *LOS*, length of stay; NA, not applicable; *IV*, intravenous; *ESI*, Emergency Severity Index; *UCC*, urgent care center.
Data are provided as No. (%) unless otherwise indicated.

Table 2. Unadjusted associations between baseline characteristics and the odds of return within 72 hours.

	Second Visit Within 72 Hours		
Characteristic	**Yes (N=3,851)**	**No (N=78,288)**	**OR (95% CI)**
Ondansetron prescription at discharge			
Yes	444 (11.5)	10,560 (13.5)	0.84 (0.76–0.92)
No	3,407 (88.5)	67,728 (86.5)	1 [Reference]
Age, median (IQR), y	3.0 (1–6)	4.0 (2–8)	0.95 (0.94–0.95)
LOS, mean (SD), min	167.7 (107.6)	159.9 (112.5)	7.8 (4.1–11.4)
Sex			
Male	1,989 (51.6)	39,714 (50.7)	1.04 (0.97–1.11)
Female	1,862 (48.4)	38,571 (49.3)	1 [Reference]
Ethnicity			
Hispanic	3,421 (90.6)	64,090 (84.6)	1.75 (1.57–1.96)
Other	354 (9.4)	11,623 (15.4)	1 [Reference]
Race			
White	3,339 (88.7)	64,734 (86.2)	1 [Reference]
Black	191 (5.1)	5,855 (7.8)	0.63 (0.55–0.73)
Other/unknown	233 (6.2)	4,528 (6.0)	1.0 (0.87–1.14)
IV access obtained during visit			
Yes	506 (13.1)	7,277 (9.3)	1.48 (1.34–1.63)
No	3,345 (86.9)	71,011 (90.7)	1 [Reference]
IV fluid bolus given during visit			
Yes	407 (10.6)	6,076 (7.8)	1.41 (1.26–1.56)
No	3,444 (89.4)	72,212 (92.2)	1 [Reference]
Any medication given during visit			
Yes	2,416 (62.6)	45,819 (58.5)	1.18 (1.11–1.27)
No	1,441 (37.3)	32,469 (41.5)	1 [Reference]
Ondansetron given during visit			
Yes	2,231 (57.9)	44,999 (56.0)	1.08 (1.01–1.15)
No	1,620 (42.1)	35,289 (44.0)	1 [Reference]
Radiologic study during visit			
Yes	611 (15.9)	10,493 (13.4)	1.22 (1.11–1.25)
No	3,240 (84.1)	67,795 (86.6)	1 [Reference]
ESI level			
2	19 (0.7)	460 (0.7)	0.81 (0.50–1.26)
3	688 (23.6)	14,060 (24.3)	0.96 (0.88–1.05)
4	2,189 (75.3)	43,118 (74.6)	1 [Reference]
Insurance			
Medicaid	2,838 (75.6)	52,791 (69.4)	1 [Reference]
Commercial	791 (21.1)	19,852 (26.1)	0.74 (0.68–0.80)
State	57 (1.5)	1,360 (1.8)	0.78 (0.59–1.01)
Self-pay	68 (1.8)	2,043 (2.7)	0.62 (0.48–0.79)
Location of initial visit			
ED	2,406 (62.5)	46,006 (58.8)	1.17 (1.09–1.25)
UCC	1,445 (37.5)	32,282 (41.2)	1 [Reference]
Treated by			
Pediatric emergency medicine physician	783 (20.3)	17,524 (22.4)	0.89 (0.82–0.96)
Pediatrician	3,067 (79.7)	60,756 (77.6)	1 [Reference]

Table 3. Predictors of 72-hour return visits in patients with gastroenteritis or vomiting.

	Unadjusted	Adjusted
Characteristic	**OR (95% CI)**	**OR (95% CI)**
Prescription of ondansetron at discharge	0.84 (0.76–0.92)	0.84 (0.75–0.93)
Age, y	0.95 (0.94–0.95)	0.95 (0.94–0.95)
Race		
White	1 [Reference]	1 [Reference]
Black	0.63 (0.55–0.73)	0.65 (0.56–0.76)
Other/unknown	1.0 (0.87–1.14)	0.98 (0.86–1.13)
IV fluid bolus during visit	1.41 (1.26–1.56)	1.48 (1.32–1.67)
Ondansetron given during visit	1.08 (1.01–1.15)	1.11 (1.04–1.19)
Radiologic study during visit	1.22 (1.11–1.25)	1.25 (1.14–1.37)
Insurance		
Medicaid	1 [Reference]	1 [Reference]
Commercial	0.74 (0.68–0.80)	0.78 (0.72–0.85)
State	0.78 (0.59–1.01)	0.99 (0.75–1.31)
Self-pay	0.62 (0.48–0.79)	0.69 (0.53–0.88)
Treated in ED (vs UCC)	1.17 (1.09–1.25)	1.11 (1.03–1.20)
Treated by **pediatric emergency** medicine physician (vs pediatrician)	0.89 (0.82–0.96)	0.86 (0.78–0.94)

The analysis performed in the subgroup of patients specifically receiving a diagnosis of gastroenteritis (55.6% of the total study sample) yielded similar results. Receiving an ondansetron prescription was associated with decreased odds of return (18%) within 72 hours. The adjusted OR was 0.82 (95% CI 0.72 to 0.95).

Six of the 11,004 patients (0.05%) who received a prescription for ondansetron had a diagnosis of appendicitis on their second visit. The risk of appendicitis was similar in patients who did not receive a prescription for ondansetron (40 of 71,135 [0.06%]; OR 0.97; 95% CI 0.37 to 2.18). A total of 16 cases of intussusception were diagnosed during return visits, all of them in patients who did not receive an ondansetron prescription. Two patients returned within 72 hours with a diagnosis of meningitis, of whom neither received an ondansetron prescription. There were no patients who returned with a diagnosis of intracranial mass or diabetic ketoacidosis.

In the subgroup of patients with gastroenteritis, 3 of those who received a prescription for ondansetron (0.05%) had appendicitis diagnosed on the second visit compared with 23 patients who did not receive a prescription for ondansetron (0.1%) (OR 0.84; 95% CI 0.19 to 2.4). There were 7 cases of intussusception diagnosed during returns visits, all of them in patients who did not receive an ondansetron prescription. None of the patients in this subgroup had a diagnosis of meningitis, intracranial mass, or diabetic ketoacidosis.

LIMITATIONS

One of the main limitations is that we were unable to assess whether patients returned to other facilities outside of our health system. Our study, however, was conducted in the largest regional pediatric health system. It includes a tertiary care center that is the only freestanding children's hospital in the county, serving 90,000 ED patients, and 11 urgent care centers serving 120,000 patients annually. The geographic locations of the centers span greater than 140 square miles in a densely populated metropolitan area and are the major referral centers in the area, so even if patients presented to other hospitals with alternate diagnoses such as appendicitis, they would typically be sent to ours.

Despite our finding of significantly decreased odds of return for patients given an ondansetron prescription, the number needed to treat was 138 because the baseline return rate was low, at 4.7%, and so the absolute difference between treated and untreated patients was small. Despite a relatively high number needed to treat, we consider our findings clinically significant, given the frequency with which patients with vomiting and gastroenteritis are treated in the ED and discharged home with or without an ondansetron prescription.

It is unknown from our data how many ondansetron doses were prescribed, whether the prescription was filled, or whether the patient used any of the prescribed medication. This does not, however, have a critical effect on the outcome measures of this study because they show

that the intention to treat with a prescription of ondansetron is associated with a reduced risk of return visits. In other words, if some patients prescribed ondansetron never received the medication, then the findings of our study would underestimate, rather than overvalue, the true effect of prescribing the medication.

Finally, there was also the limitation of residual confounding because of variables that we were not able to measure and control for. As an example, patients received their care at the discretion of the treating physician, and there may have been unmeasured clinical differences between patients that accounted for the provision of a particular treatment, including prescribing ondansetron for home use. This limitation is unavoidable for all studies based on observational designs. Only conducting a prospective randomized controlled trial can circumvent this constraint.

DISCUSSION

In this large historical cohort study including 82,139 patients with vomiting or gastroenteritis, we found that receiving an ondansetron prescription was associated with decreased odds of 72-hour return visits to the ED or urgent care center. Similar findings were observed in the subgroup of patients specifically receiving a diagnosis of gastroenteritis. Finally, we found that a prescription of ondansetron did not increase the risk of patients' returning with an alternate diagnosis, such as appendicitis or intussusception.

Previous studies have established the effectiveness of ondansetron given in the pediatric ED, as demonstrated by its aiding oral rehydration and decreasing admission rates.[5,14] Our study adds to this existing knowledge by suggesting that prescribing ondansetron may help with oral rehydration for patients who continue to have episodes of vomiting at home, and receiving an ondansetron prescription may contribute to decreased return rates. Two recent studies, however, examining the association of an ondansetron prescription with return rates to the pediatric ED showed no difference in return rates for patients prescribed ondansetron for home versus those who were not.[9,15] Several factors could explain why their results differed from ours. In their study, Gray et al[9] applied a different methodology using Fisher's exact test to compare return rates, which does not adjust for confounders, whereas we used logistic regression for that purpose. Their population demographics were different from ours, consisting of more black patients (49% versus 5.4%) and fewer Hispanic ones (11% versus 83.4%). They had higher prescription rates of ondansetron (71% versus 13.4%), and their small sample size (996 patients with acute gastroenteritis) may have limited their ability to identify any existing differences in return rates between groups. In the study by McLaren et al,[15] although they applied methodology similar to that of our study by using a logistic regression model, different results were obtained. This could be due to the use of different variables in our model or that we had a larger sample size (82,135 versus 11,785) with associated narrower CIs, which increased the precision of our point estimate. Another possible reason for the differences in results is various population demographics, with significantly more Hispanic patients in our study (83.4% versus 24.8%). Additionally, their study had higher prescription rates (35.1% versus 13.4%), which suggests either a difference in clinical characteristics between the 2 study populations or differences in physicians' decision to treat. Finally, we do not know whether other important unmeasured differences existed, such as education level of parents, patient access for follow-up with pediatricians, or baseline patterns of ED utilization.

In addition to patients with a specific diagnosis of gastroenteritis, we also included those with diagnoses of vomiting or gastritis for 2 reasons. First, the initial presentation of gastroenteritis is frequently with vomiting alone, and patients are often evaluated in the ED before the start of diarrhea; thus, we included *ICD* codes of vomiting or acute gastritis. Second, there are many other benign causes of vomiting in addition to gastroenteritis in which ondansetron is prescribed, making our results more applicable to situations that physicians face daily. Because of our decision to include other causes of vomiting, we analyzed the subgroup of patients specifically receiving a diagnosis of gastroenteritis and found results similar to that of our total population.

We did not limit our study sample to only patients treated in the ED, but also included patients treated in the urgent care centers affiliated with our hospital system. Even though it is possible that these patients were less sick than those treated in the ED, including them made our study findings more generalizable to a wide variety of practices because many patients are treated in urgent care centers for similar complaints.

In our study, baseline characteristics between patients who received an ondansetron prescription and those who did not were statistically different. These findings are not surprising, given the fact that this was an observational study and patients were not randomized. In addition, the large sample size may have rendered statistically significant differences that may not be clinically meaningful. We attempted, however, to identify and correct for possible confounders particularly related to severity of disease and

took into consideration several potential markers of severity when developing our logistic regression model. These markers included Emergency Severity Index level, intravenous access obtained during visit, intravenous fluid bolus given, radiologic studies obtained, and medications given during the visit, including ondansetron, and were chosen a priori in accordance with our clinical experience, in which we believed that the above-mentioned markers or interventions were anecdotally associated with more severe illness.

Previous studies have evaluated the possibility of masking alternate diagnoses when patients are given ondansetron for vomiting in the ED.[16,17] Sturm et al[16] found that patients receiving ondansetron in the ED had an increased risk for return within 72 hours, but it was not associated with masking an alternate diagnosis on return. These studies, however, assessed patients who were given ondansetron in the ED and did not focus primarily on those prescribed ondansetron on discharge. From our institutional experience, we know that physicians are wary about prescribing ondansetron for home use because of concern about masking alternate diagnoses, as suggested by their comparatively low prescribing rates (13.4%). Our study data suggest that receiving a prescription for ondansetron is not associated with an increased risk of alternate diagnoses such as appendicitis on return visit. A concern may be raised about delaying the diagnosis of appendicitis by prescribing ondansetron for home use because patients may return later with possible complications such as a perforated appendix. To evaluate this concern, we performed a chart review on cases of appendicitis and noted that of the patients who returned, 13 had a diagnosis of perforated appendicitis, of whom 3 had received a prescription for ondansetron. Two of these patients returned within 1 day of the index visit, and the third patient returned after 4 days.

All cases of intussusception were observed in patients who did not receive a prescription for ondansetron; therefore, it was not possible to compare rates for this condition between the 2 groups. Finally, frequencies of other diagnoses were too low to warrant any meaningful conclusion. There were 2 patients who returned with a diagnosis of meningitis, neither of whom received a prescription for ondansetron, and no patients returned with a diagnosis of intracranial mass or diabetic ketoacidosis. Even though we cannot make any statistical conclusions in regard to these patients, our large study sample demonstrates the rarity of these disease events whether a prescription for ondansetron was given or not, and that the risk of missing a serious diagnosis is very low.

This study did not evaluate whether patients who received ondansetron and returned had higher rates of diarrhea, which is a known adverse effect of the drug.[18] Making this distinction, however, is probably not necessary because the prescription for ondansetron was associated with a reduced risk for return despite this potential adverse effect.

In summary, we found that receiving an ondansetron prescription is associated with reduced 72-hour return visits for children with vomiting or gastroenteritis and is not associated with masking alternate diagnoses. Despite a relatively large number needed to treat, we believe this is clinically significant because of the large proportion of patients who are treated in the ED for these complaints. As ED volumes increase nationally, with potential systemwide ramifications, measures that can be taken to safely mitigate this problem should be considered. Prospective studies are needed to evaluate the direct effect of ondansetron prescription on return visits to the ED.

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